



*Journal of Applied Pharmaceutical Research*  
Volume 5, Issue 3, Year of Publication 2017, Page 1 – 7  
DOI: 10.18231/2348-0335.2017.0001



## Review Article

**JOURNAL OF APPLIED PHARMACEUTICAL RESEARCH | JOAPR**

www.japtronline.com

ISSN: 2348 – 0335

### ACNE: CURRENT PERSPECTIVE

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#### Article Information

Received: 25<sup>th</sup> May 2017

Revised: 10<sup>th</sup> June 2017

Accepted: 17<sup>th</sup> June 2017

#### Keywords

Topical, acne, dermatology, retinoids

#### ABSTRACT

*Acne vulgaris* or acne is a multi factorial chronic inflammatory disease of pilosebaceous unit. Globally it affects approximately 9.4% of the population. It is characterized by blackheads and white heads, pinheads, large papules which may lead to scarring. Other than scarring, its main effects are psychological, such as distress and reduced self-esteem. Up to 80% of teenage girls and 90% of teenage boys are afflicted with acne. Adult acne, although less common than adolescent acne, is a significant problem for 3% to 6% of adult men and 5% to 12% of adult women. It is the most common chronic skin disorders which require urgent attention. Successful treatment of acne requires careful selection of anti-acne agents.

#### INTRODUCTION

*Acne vulgaris* is a common chronic skin disease involving blockage and/or inflammation of pilosebaceous units (hair follicles along with sebaceous gland) [1]. It appears as non inflammatory lesions such as microcomedones and inflammatory lesions such as papules and pustules or a mixture of both. It mainly affects the areas of skin with the densest population of sebaceous follicles eg. face, upper chest and back [2]. The individuals may also suffer with severe nodular acne

which may lead to pain as well as both physical and psychological scarring. Apart from scarring, its main effects include social embarrassment, reduction in self-confidence [3] and in very extreme cases, depression or suicide [4]. One study has estimated the incidence of suicidal ideation in patients with acne as 7.1% [5]. Acne affects mainly during adolescence, It was estimated that approximately 80–90% of teenagers are affected with acne [6-8]. Low rates are reported in rural societies [9]. In 2010 it was estimated to be the 8th most

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common disease globally affecting 650 million people [10]. Although acne diminishes over time and tends to decline by age of 25 [11] but some individuals remain affected beyond their thirties and forties [12]. Successful management of acne needs careful selection of anti-acne agents according to clinical presentation and individual patient needs [13][14]

## SYMPTOMS OF ACNE

Acne vulgaris (or simply acne) is characterized by [15] :

- areas of seborrhea (scaly red skin),
- comedones (blackheads and whiteheads),
- papules (pinheads), nodules (large papules),
- pimples and ultimately scarring.

Other symptoms may include pain, tenderness or erythema depending upon the severity of disease.



Figure 1: acne on back [16]



Figure 2 :Acne on face [17]

Systemic symptoms are most often absent in acne vulgaris. Severe acne with associated systemic signs and symptoms, such as fever, is referred to as acne fulminans. Severe acne, characterized by multiple comedones, without the presence of systemic symptoms, is known as acne conglobata. This severe form of acne frequently heals with disfiguring scars. Moreover acne has psychological impact depending on the severity or grade of the disease [18]

## TYPES OF ACNE (On the basis of diagnosis)

On the basis of diagnosis and severity of condition acne can be classified as mild, moderate, or severe [2]. It includes:

- **Comedonal acne:** This may be characterized by presence of open (blackheads) and closed (whiteheads) comedones but no signs of any inflammatory papules or nodules.
- **Mild acne:** It includes the presence of comedones with occasionally inflammatory lesions. Open and closed comedones mostly limited to the face [2]
- **Moderate acne:** It includes presence of comedones, inflammatory papules and pustules. Inflammatory lesions are more than in mild inflammatory acne and these involve face as well as the trunk of the body [2]
- **Severe nodular acne:** It may be characterized as presence of comedones, inflammatory lesions, and large nodules. These nodules (the painful 'bumps' lying under the skin) are generally greater than 5 mm in diameter. These may also lead to scarring. The nodules are present on face and trunk. These were also considered cysts so this type is also termed as nodulocystic acne [19]

## CAUSES OF ACNE

Acne appear mostly in young people due to several factors [22]

- hormonal imbalances (overproduction of the male sex hormones),
- bacterial infection,
- heredity or genetics,
- consumption of certain drugs (including androgens and barbiturates)
- exposure to environmental irritants (such as pollution and high humidity),
- stress,
- cosmetic application,
- squeezing or picking at blemishes,
- Hard scrubbing of the skin.

Increase in hormonal activities especially during puberty, may cause the formation of acne. The most important cause attributed is infections due to *Propionibacterium acnes* (*P. acnes*), the anaerobic bacterium species [23]



Figure 3: A severe case of nodular acne [20]



Figure 4: Nodular acne on the back [21]

### INCIDENCE OF ACNE

Acne is a common condition which affects millions of adolescents and adults. Adult acne is less common than adolescent acne. But, still it is a problem for 3% to 6% of adult men and 5% to 12% of adult women. It was estimated that acne affects 54% of women and 40% of men older than 25 years of age [24][25]. In those over 40 years old, 1% of males and 5% of females still have problems [2]. In 2013, acne was estimated to affect 660 million people globally, making it the 8<sup>th</sup> most common disease worldwide [26] - [29]. It is slightly more common in females than males (9.8% versus 9.0%) [30]. Although the presence of acne does not physically impair patients, it can have a remarkable psychological effect. Thirty to fifty percent of adolescents experience psychiatric disturbances as the result of acne. While some research has found it affects people of all ethnic groups [28]. The social and economic costs of treating acne vulgaris are substantial. In the United States, *Acne vulgaris* is responsible for more than 5 million doctor visits and costs over US\$2.5 billion each year in direct costs. Similarly, acne vulgaris is responsible for 3.5 million doctor visits each year in the United Kingdom [2]. The FDA has issued a warning that certain over the counter topical acne products may cause rare but serious and potentially life threatening allergic reactions or severe irritation. Users who experience hypersensitivity reactions such as throat tightness, difficulty in breathing, feeling faint or swelling of the eyes, face, lips or tongue or who develops hives or itching should stop using the products and seek immediate emergency medical attention [31][32]

### PATHOGENESIS OF ACNE

The pathogenesis of acne vulgaris is multifactorial. The key factor is genetics [33]. Acne develops due to following four factors: [34]

- Release of inflammatory mediators into the skin
- Follicular hyperkeratinization and then plugging of the follicle

- follicular colonization of *Propionibacterium acnes*
- Excess sebum production

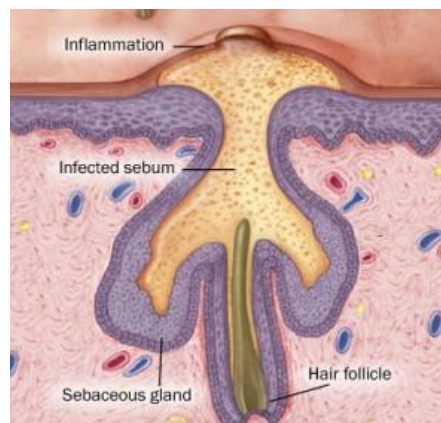


Figure 5: Acne pathogenesis [35]

It was found that the inflammatory responses occur before hyper keratinization. Cytokines and macrophages regulate inflammatory mediators such as vascular cell adhesion molecule-1 (VCAM-1), intercellular adhesion molecule-1 (ICAM-1), and human leukocyte antigen (HLA)–DR in the vessels around the pilosebaceous follicle [36]. Follicular hyperkeratinization involves increased keratinocyte proliferation and decreased desquamation, leading to sebum- and keratin-filled microcomedones [37]

*P. acnes* is an anaerobic organism present in acne lesions. The presence of *P. acnes* promotes inflammation through a variety of mechanisms. *P. acnes* stimulate inflammation by producing proinflammatory mediators that diffuse through the follicle wall. Studies have shown that *P. acnes* activate the toll-like receptor 2 on monocytes and neutrophils [38]. Activation of the toll-like receptor 2 then leads to the production of multiple proinflammatory cytokines, including interleukins 12 and 8 and tumour necrosis factor. Hypersensitivity to *P. acnes* may also explain why some individuals develop inflammatory *Acne vulgaris* while others do not [39].

Excess sebum is another key factor in the development of *Acne vulgaris*. Sebum production and excretion are regulated by a number of different hormones and mediators. In particular, androgen hormones promote sebum production and release [40]. The degree of comedonal acne in prepubertal girls correlates with circulating levels of the adrenal androgen dehydroepiandrosterone sulfate (DHEA-S) [41]. Numerous other mediators and receptors, including growth hormone and insulinlike growth factor, as well as peroxisome proliferator-activated receptors also regulate the sebaceous gland and may

contribute to the development of acne [42][43]. Furthermore, the sebaceous gland acts a neuroendocrine-inflammatory organ that is activated via corticotrophin-releasing hormones in response to stress and normal functions [44]

## DIAGNOSIS

Several scales exist to grade the severity of *Acne vulgaris*, but no single technique has been universally accepted as the diagnostic standard [45][46]. Cook's acne grading scale uses photographs to grade severity from 0 to 8 (0 being the least severe and 8 being the most severe) [46]. Leeds acne grading technique counts acne lesions on the face, back, and chest and categorizes them as inflammatory or non-inflammatory. Leeds scores range from 0 (least severe) to 10 (most severe) though modified scales have a maximum score of 12 [46][47]. The Pillsbury acne grading scale simply classifies the severity of the acne from 1 (least severe) to 4 (most severe) [45][48]

## ACNE TREATMENT

In the present scenario various therapies include:

**Topical Therapy** includes benzoyl peroxide available in different formulations such as washes, lotions, creams, and gels with concentrations (2.5–10%). It does not cause bacterial antibiotic resistance like antibiotics [49]. However topical retinoids such as tretinoin, adapalene, isotretinoin, metretinide, retinaldehyde, tazarotene, and  $\beta$ -retinoylglucuronide are currently used [50]. In Combination therapy Benzoyl peroxide [12] is used with topical erythromycin or clindamycin. Benzoyl peroxide could also be used with tretinoin and considered superior. Topical retinoid in combination with topical antimicrobial is found to be more effective in reducing both inflammatory and non inflammatory acne lesions.

**Systemic therapy:** For moderate to severe inflammatory acne oral antibiotics such as tetracyclines are used currently. Macrolides, co-trimoxazole, and trimethoprim are other alternatives for acne. Cephalosporins and sulphonamide, should not be used in acne due to lack of efficacy and safety. Gastrointestinal upset and vaginal candidiasis are most common side effects. Isotretinoin is an oral retinoid and is found to be very effective for severe nodular acne [2][51]. It requires one to two months of isotretinoin therapy for severe nodular acne. It takes a 4–6 month to treat acne completely by the use of oral isotretinoin [51]. After a single course, about 80% of people report an improvement, with more than 50% reporting complete remission [2]. About 20% of people require

a second course [2]. There is no clear evidence that use of oral retinoids increases the risk of psychiatric side effects such as depression and suicidality [2][51]. Isotretinoin use in women of childbearing age is strictly regulated due to its known harmful effects in pregnancy [2]. For a woman of childbearing age to be considered a candidate for isotretinoin, she must have a confirmed negative pregnancy test and use an effective form of birth control [2]

**Harmonal therapy** may be needed in female patients with severe seborrhoea, clinically apparent androgenetic alopecia, seborrhea /acne /hirsutism /alopecia (SAHA) syndrome, late-onset acne (acne tarda), and with proven ovarian or adrenal hyperandrogenism. The main approach of hormonal therapy in acne is to prevent the effects of androgens on the sebaceous gland and probably follicular keratinocytes as well. Oral antiandrogen like spironolactone and cyproterone acetate can be useful in the treatment of acne.

**Physical Treatment:** Both open and closed comedones can be removed with comedone extractor, a fine needle or a pointed blade mechanically. Topical retinoid application before this procedure makes it easier. Gentle cautery and laser puncture of macro comedones can also be done. The limitations include incomplete extraction, refilling, and the risk of tissue damage.

## ACNE SCARS

Acne scars are caused by abnormal healing followed by inflammation within the dermal layer of skin. It is estimated to affect 95% of people with *Acne vulgaris* [52]. It is most likely to take place with severe nodular acne, but may occur with any form of *Acne vulgaris* [52]. Acne scar can be broadly divided into two groups, those involving tissue losses (Ice pick scar, Box scar, Rolling scar, and Follicular macular atrophy) and those involving tissue excess (hypertrophic scars or keloids).

Ice-pick scars are narrow (less than 2 mm across), deep scars that extend into the dermis. Boxcar scars are round or ovoid indented scars with sharp borders and vary in size from 1.5–4 mm across [52]. Rolling scars are wider than ice pick and boxcar scars (4–5 mm across) and have a wave-like pattern of depth in the skin [52]

Hypertrophic scars are characterized by increased collagen content after the abnormal healing response [52]. They are described as firm and raised from the skin [52][53].

Hypertrophic scars remain within the original margins of the wound, whereas keloid scars can form scar tissue outside of these borders [52].

Keloid scars from acne occur more often in men and people with darker skin, and usually occur on the trunk of the body [52]. Currently available treatment for scars include simple excision, and suturing, either alone or combined with punch grafting and laser resurfacing, dermabrasion, various type of lasers, chemical peels, and fillers. For hypertrophic scars, treatment includes pressure therapy, IL corticosteroid, 5-fluorouracil and bleomycin injections, surgical excision, radiotherapy, laser therapy and cryotherapy. All the procedures have their own merits and demerits; to be chosen carefully seeing the merit [53]

### ACNE AND DIET

Dietary restriction has not been proved to be of any benefit in the treatment of acne. It is a myth that diet affects acne but studies are not supporting it. Various authors are still claiming that there is the definite role of diet in acne but to conclude that further controlled trials are needed. It was considered that low occurrence of acne in rural, and non industrialized societies are may be due to lower glycemic index diet.

### CONCLUSION

Acne is characterized by blackheads, whiteheads and inflammatory papules which mainly affects adolescents. Adolescent stage is a complex life cycle characterized by many biological, physical, psychological and social changes. The physical changes of acne may have negative effect on the psychology, quality of life and self-esteem of adolescents. Although many oral and topical medical agents have been found to be effective in the treatment of acne, the prevalence of the disease make the development of alternative therapies highly desirable. There has been significant progress over the past few years, but not all developments can be universally applied.

### FINANCIAL ASSISTANCE

Nil

### CONFLICT OF INTEREST

The authors declare no conflict of interest

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